REMARKS

The Office Action mailed October 22, 2003, set a three-month statutory period for response expiring January 22, 2004. Pursuant to the accompanying Petition for Extension of Time under 37 C.F.R. 1.136(a), the period for response is extended to April 22, 2004. This amendment is therefore timely filed.

Claims 1-4, 6-9, and 11-34 are in the application.

Claims 24 and 34 are withdrawn from consideration as being drawn to non-elected subject matter.

Claim 15 is amended to remove the quotation marks from the term "stepped".

Claim 17 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite on the grounds that the term "other' renders the claim indefinite because the claim includes elements not actually disclosed, i.e., those encompassed by "other", thereby rendering the scope of the claim unascertainable. Applicants disagree.

Claim 17 depends from claim 16, which is directed to a dosage form wherein the delayed release core is combined with another entity, the release of which is immediate or sustained. Accordingly, the "other" entity in claim 17 refers to the immediate or sustained release entity referred to in claim 16. Claim 17 further limits the immediate or sustained release entity to one containing an active ingredient that is different from the active ingredient in the delayed release entity. There is nothing indefinite about claim 17, and it is therefore in full compliance with 35 U.S.C. § 112. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 1, 3, 7, 9, and 11-15 are rejected under 35 U.S.C. § 102(b) as being anticipated by Heinicke et al., U.S. Patent 5,834,024. The rejection is believed overcome by the amendment of claim 1 to incorporate the limitations of claim 2, more particularly defining the surfactant type,

and by specifying the surfactant amount, support for which is found in the specification, for example, at page 6, lines 7-9. Claim 2 is not anticipated by Heinicke and hence claim 1, as amended, is likewise not anticipated. Claim 3 as amended, and claims 7, 9, and 11-15, which depend directly or ultimately from claim 1, also are not anticipated. Withdrawal of the rejection under 35 U.S.C. § 102 is requested.

Claims 1-4, 6-9, 11-23, and 25-33 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Andrieu et al., U.S. Patent 5,589,190, in view of Wilson et al., U.S. Patent 6,403,597, on the basis that Andrieu discloses a pharmaceutical composition comprising an alfuzosin hydrochloride core that is coated with methacrylic acid copolymer (EUDRAGIT) (abstract), and that the formulation comprises tablets which afford immediate or sustained release or microparticles which provide immediate release of alfuzosin (columns 1-3 and claims 1-10). While acknowledging that Andrieu fails to teach the presence of surfactant in the alfuzosin formulation, the Examiner maintains that Wilson teaches a formulation that comprises alfuzosin and surfactant (abstract, column 5, lines 39-44, column 6, lines 1-5, and column 12, line 40), and therefore relies on Wilson for the teaching that alfuzosin formulations can have surfactants. The Examiner maintains that there is no demonstration in Applicants' specification that the specific recited surfactants provide unusual results; and that one surfactant may be substituted for another surfactant without affecting the novel characteristics of the invention. The Examiner concludes it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare alfuzosin formulation as disclosed by Andrieu, and that one having ordinary skill in the art would have been motivated to incorporate surfactant in the alfuzosin formulation with the expectation that the presence of the surfactant would facilitate the dissolution of alfuzosin. The rejection is respectfully traversed and reconsideration thereof is requested.

Andrieu discloses a composition containing an alfuzosin hydrochloride core coated with a pH-dependent polymer which dissolves at a pH above 7, namely, Endragit® S, which, as shown on the attachment hereto, is an anionic polymer of methacrylic acid and methacrylates with a carboxyl group. Applicants' compositions are coated with ammonia methacrylate copolymers, e.g., Eudragit® RL and Eudragit® RS, which are pH-independent copolymers of acrylate and methacrylates with quaternary ammonium groups. As shown on the attachment, Eudragit® RL is an insoluble, high-permeability, pH-independent polymer, and Eudragit® RS is an insoluble, low-permeability, pH-indpendent polymer. Thus, the structure and properties of the polymer coatings of Applicants' compositions differ substantially from those of Andrieu, and clearly, nothing in Andrieu would have suggested using Applicants' ammonio methacrylate polymer to produce a delayed release formulation. Furthermore, as acknowledged by the Examiner, Andrieu fails to teach the presence of a surfactant in its composition, and Wilson is relied upon for teaching that alfuzosin formulations can have surfactants. It is submitted that this characterization of the teaching of the Wilson reference amounts to picking and choosing from the reference only that which supports the Examiner's position and is not a fair representation of what the reference as a whole would teach one of ordinary skill in the art. Wilson does not, in fact, teach any formulation containing any surfactant; nor does it teach any formulation containing alfuzosin. Wilson broadly discloses virtually every known type of pharmaceutical formulation containing an active agent selected from a list of compounds stretching over seven columns of the patent (columns 8-14) in combination with an unspecified carrier or vehicle and virtually any other component known to those skilled in the art of pharmaceutical formulation preparation and drug delivery (column 5, lines 34-43). The fact that the words alfuzosin and surfactants are found in the Wilson patent is simply not tantamount to a teaching of an alfuzosin composition containing a surfactant, let alone the surfactants defined in Applicants' claims.

Moreover, there is nothing in Wilson to suggest what effect a surfactant might have on the properties of the Andrieu compositions, and even if Wilson were competent to suggest adding a surfactant to the composition of Andrieu, given the differences in the Andrieu compositions and Applicants' compositions as explained above, there is nothing in the cited references to suggest that any beneficial properties would be realized by including a cationic or zwitterionic surfactant in Applicants' compositions.

The Examiner maintains that there is no demonstration in Applicants' specification that the recited surfactants provide unusual results. In fact, the specification teaches precisely that. The dissolution properties of Example 1 containing a cationic surfactant were compared with those of comparative example 1 from which the cationic surfactant was omitted. As shown in Figures 2 and 3, Example 1 released 80% of the alfuzosin over 20 hours whereas comparative example 1 had released less than 50%. Likewise, the dissolution properties of Example 3 containing a zwitterionic surfactant were compared with those of comparative example 3 without zwitterionic surfactant. Figures 5 and 6 show that Example 3 exhibited a delayed release in which about 70% of the alfuzosin had been released after six hours and nearly 100% had been released after 16 hours whereas comparative example 3 exhibited a gradual release in which about 30% of the alfuzosin had been released after six hours and about 80% had been released after 16 hours. Thus, the surfactant gave a delayed accelerated pulse and substantially more complete release of the drug. Clearly, nothing in the cited references would have suggested this effect.

In view of the foregoing, it is submitted that the Andrieu and Wilson references taken individually or in combination are incompetent to teach or suggest the invention here claimed, and accordingly, the rejection based thereon should be withdrawn.

There being no remaining issues, this application is believed in condition for favorable reconsideration and early allowance, and such actions are earnestly solicited.

Respectfully submitted,

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EXCIPIENTS

METHACRYLATE-BASED COATINGS

*1] **Description:*** Methacrylate-based coating materials with a variety of functional properties.

Functionality	Trade name
Anionic polymer of methacrylic acid and methacrylates with a -COOH group	Eudragit® L 100-55 - powder, spray dried L 30 D-55 which can be reconstituted for targeted delivery in the duodenum Eudragit® L 30 D-55 - aqueous dispersion, pH dependent polymer soluble above pH 5.5 for targeted delivery in the duodenum Eudragit® L 100 - powder, pH dependent polymer soluble above pH 6.0 for targeted delivery in the jejunum Eudragit® S 100 - powder, pH dependent polymer soluble above pH 7.0 for targeted delivery in the ileum. Eudragit® FS 30 D - aqueous dispersion, pH dependent polymer soluble above pH 7.0, requires no plasticizer
Cationic polymer with a dimethylaminoethyl ammonium group	Eudragit E 100 - granules, pH dependent, soluble in gastric fluid up to 5.0, swellable and permeable above pH 5.0. Eudragit® E PO - powder form of E-100
	Insoluble, High Permeability Eudragit® RL 30D - aqueous dispersion, pH independent polymer for sustained release formulations Eudragit® RL PO - powder, pH independent polymer for matrix formulations

Copolymers of acrylate and methacrylates with quarternary ammonium group.	Eudragit® RL 100 - granules, pH independent **Insoluble, Low Permeability** Eudragit® RS 30D - aqueous dispersion, pH independent polymer for sustained release formulations Eudragit® RS PO - powder, pH independent polymer for matrix formulations Eudragit® RS 100 - granules, pH independent
Copolymers of acrylate and methacrylates with quarternary ammonium group in combination with sodium carboxymethylcellulose	Eudragit RD 100 - powder, pH independent for fast disintegrating films

2) Applications:

Enteric Coatings	Eudragit® L 100-55 or L 30 D-55 - delivery to the duodenum (pH > 5.0). Exact pH controlled drug release can be adjusted by a combination of polymers and coating thickness. Eudragit® L 100 - delivery to the jejunum (pH > 6.0). Eudragit® S 100 - delivery to the intestine (pH 6.0 to 7.5), site specific drug delivery can be achieved by combining with Eudragit® L types. Eudragit® FS 30 D - delivery to the colon (pH >7.0).
Sustained Release Coatings	Eudragit® RL and RS - release profile determined by the ratio of RL to RS polymers, and the film thickness applied.
Taste Masking	Eudragit® RD 100, pH independent, fast disintegrating film Eudragit® E 100 and EPO, pH dependent cationic polymer, soluble in gastric fluid up to pH 5.0, swellable and permeable above pH 5.0